enhance these protective effects in the hearts of diabetic rats. Chronic Resveratrol treatment with Ipost neither reduced infarct size nor increased myocardial dysfunction recovery in both diabetic and non-diabetic rats (infarct size: 59.5% and 59.2% in diabetic ones and 45.0% and 43.7% in non-diabetic ones, P>0.05, respectively), and this might be associated with an inhibition of Akt and eNOS phosphorylation.
Conclusions: The combination of acute Resveratrol treatment with Ipost shows a stronger protective effect within the hearts of diabetic rats, but chronic Resveratrol with Ipost fails to protect hearts against reperfusion injury in either diabetic or non-diabetic rat hearts. These findings will be important for the design of future clinical investigations.

GW25-e3108

Deletion of TRPV1 Accelerates DOCA-salt Hypertension-induced Renal Injury via Activation of CCR2

Youping Wang, Mingjun Zhu, Lin Cui, Weihong Liu, Xiaoxiao Wang, Shiyang Xie, Si Shen
Central Laboratory and Division of Cardiology, First Affiliated Hospital, Henan University of Traditional Chinese Medicine, Zhengzhou, 450000, China

Objectives: Our studies demonstrate that deletion of the transient receptor potential vanilloid type 1 (TRPV1) gene aggravates deoxycorticosterone acetate (DOCA) -salt hypertension-induced renal injury, which is associated with increased intra-renal monocyte/macrophage infiltration and inflammation. The results suggest that TRPV1 may act as a potential regulator of monocyte/macrophage infiltration to reduce renal injury in DOCA-salt hypertension. Therefore, this study was designed to test the hypothesis that deletion of TRPV1 exaggerates salt-sensitive hypertension-induced renal injury via activation of chemokine receptor 2 (CCR2).
Methods: We induced salt-sensitive hypertension for 4 weeks by uninephrectomy and DOCA-salt in wild type (WT) and TRPV1-null mutant ($TRPV1^{-/-}$) mice with or without the selective CCR2 antagonist, RS504393.
Results: DOCA-salt treatment increased systolic blood pressure (SBP) to the same degree in both strains, but increased urinary excretion of albumin and 8-isoprostane and decreased creatinine clearance with greater magnitude in $TRPV1^{-/-}$ mice compared to WT mice (89.3±5.2 vs. 26.5±3.4 μg/24h; 4.24±0.45 vs. 1.52±0.21 ng/24h; 98±19 vs. 168±14 ml/24h, P<0.05). DOCA-salt treatment also caused renal glomerulosclerosis, tubulointerstitial injury, collagen deposition, monocyte/macrophage infiltration, proinflammatory cytokine and chemokine production, and NF-κB activation in greater degree in $TRPV1^{-/-}$ mice compared to WT mice (glomerulosclerosis index: 0.78±0.15 vs. 0.35±0.14; tubulointerstitial injury score: 3.37±1.0 vs. 2.01±0.49; collagen content: 21.8±2.3 vs. 13.8±2.4 μg/mg dry tissue; monocyte/macrophage infiltration: 74±4 vs. 42±5 cells/mm^2; TNF-α: 1.03±0.22 vs. 0.76±0.21 pg/mg protein; MCP-1: 10.35±1.19 vs. 6.00±0.86 pg/mg protein; p65-NF-κB protein: 54±5 vs. 36±3 ng/mg protein, P<0.05). Blockade of the CCR2 with RS504393 (4 mg/kg) had no effect on SBP in DOCA-salt-treated WT or $TRPV1^{-/-}$ mice compared to their respective controls. However, treatment with RS504393 ameliorated renal dysfunction and morphological damage, and prevented the increase in monocyte/macrophage infiltration, cytokine/chemokine production, and NF-κB activity in both DOCA-salt hypertensive strains with a greater effect in DOCA-salt-treated $TRPV1^{-/-}$ compared to DOCA-salt-treated WT mice.
Conclusions: Our study showed that blockade of CCR2 with RS504393 attenuated DOCA-salt hypertension-induced renal injury in WT and $TRPV1^{-/-}$ mice independently of their effects on blood pressure. The protective effect was greater in $TRPV1^{-/-}$ mice compared to WT mice. The results suggest that deletion of TRPV1 aggravated salt-sensitive hypertension-induced renal damage possibly via activation of the MCP-1/CCR2 signaling pathway. [This work was supported by a grant from the National Natural Science Foundation of China (No. 81170243)].

GW25-e3129

β1-Adrenergic receptor-mediated HO-1/HMGB1 axis via PI3K and p38 MAPK attenuates rat myocardial ischemia/reperfusion injury in vivo

Wang Jichun, Hu Xiaorong, Xie Jing, Zhou Xiaoya, Jiang Hong
Department of Cardiology, Renmin Hospital of Wuhan University, Cardiovascular Research Institute of Wuhan University, Wuhan, PR China

Objectives: It has been reported that the induction of heme oxygenase-1 (HO-1) mediated by β1-adrenergic receptor inhibits high mobility group box 1 protein (HMGB1) release and increases the survival rate in cecal ligation and puncture-induced septic mice. The present study aimed to investigate whether dobutamine, a selective β1-adrenergic receptor agonist, could inhibit HMGB1 release via β1-adrenergic receptor-mediated HO-1 induction and attenuate myocardial ischemia/reperfusion (I/R) injury in rats.
Methods: Anesthetized male rats were pretreated with dobutamine (5 or 10 microg.Kg-1. min-1, intravenous) before ischemia in the absence and/or presence of LY294002 (0.3 mg/Kg), a phosphatidylinositol 3-kinase (PI3K) inhibitor; SB203580 (1 mg/Kg), a p38 mitogen-activated-protein kinase (P38 mitogen-activated-protein kinase [p38 MAPK]) inhibitor, and zinc protoporphyrin IX ([ZnPPIX], 10 mg/Kg), a HO-1 inhibitor, respectively, and then subjected to ischemia for 30 min followed by reperfusion for 4 h. The myocardial I/R injury and oxidative stress were assessed. Likewise, the expressions of HO-1 protein, nuclear factor kappa B (NF-kappaB) p65, and HMGB1 were measured by Western blot analysis.
Results: After 4 h reperfusion, compared with I/R group, the pretreatment of dobutamine significantly reduced the infarct size in a dose-dependent manner, and the increase of LDH and CK levels were significantly inhibited by dobutamine (both P<0.05 versus I/R group). Meanwhile, dobutamine dose-dependently reduced oxidative stress by inhibiting the increase of the MDA level and the decrease of the SOD level (both P<0.05 versus I/R group). Otherwise, dobutamine produced a statistically significant reduction in the production of TNF-α and IL-6 compared with the I/R group (both P<0.05 versus I/R group). Furthermore, compared with I/R group, dobutamine significantly and dose-dependently mediated HO-1 induction and NF-kappaB p65 and HMGB1 inhibition (all P<0.05 versus I/R group). However, all the effects caused by dobutamine were significantly reversed by the presence of LY294002, SB203580, and ZnPPIX, respectively.
Conclusions: The present study demonstrated that dobutamine mediated the induction of HO-1 by selectively stimulating β1-adrenergic receptor via PI3K and p38 MAPK, which inhibited HMGB1 release and attenuated rat myocardial I/R injury in vivo.

GW25-e3132

Single nucleotide Polymorphism of the CYP2J2 Gene is Associated with Essential Hypertension in Uygur Population in China

Zhu Qing[1,2], Fu Zhen-yan[1,2], Ma Yi-tong[1,2]
[1]Department of Cardiology, First Affiliated Hospital of Xinjiang Medical University, Urumqi, People's Republic of China, [2]Xinjiang Key Laboratory of Cardiovascular Disease Research, Urumqi, People's Republic of China

Objectives: Human Cytochrome P450 2J2 (CYP2J2) is the major arachidonic acid epoxygenase, which can metabolizes arachidonic acid (AA) to biologically active epoxyeicosatrienoic acids (EETs). The EETs are potent endogenous vasodilators and inhibitors of vascular inflammation. Recently, much evidence from models and human studies suggests that variability of CYP2J2 gene plays a mechanistic role in the development of hypertension. The aim of the present study was to assess the association between the human CYP2J2 gene polymorphism and Essential Hypertension (EH) in a Han and Uygur population in China.
Methods: We used two independent case-control studies: a Han population (302 EH patients and 300 control subjects) and a Uygur population (567 EH patients and 215 control subjects). All EH patients and controls were genotyped for the same three single nucleotide polymorphisms (SNPs) (rs890293, rs11572223 and rs2280275) of CYP2J2 gene by a Real-time PCR instrument.
Results: In the Uygur population, the distribution of SNP3 (rs2280275) genotypes, alleles and the dominant model (CC vs CT + TT) showed a significant difference between EH and control participants (for genotype: P=0.007; for allele: P=0.001; for dominant model: P=0.002). The significant difference in dominant model was retained after adjustment for covariates (OR: 3.500, 95% confidence interval [CI]: 1.680-7.300, P=0.001). However, all the above differences were not shown in the Han population.
Conclusions: The CC genotype of rs2280275 in CYP2J2 gene could be a risk genetic marker of EH and T allele may be a protective genetic marker of EH in Uygur population in China.

GW25-e3140

Endothelial cells induced by inflammation release multiple angiogenesis-associated microRNAs into circulation through microparticles

Zhang Jing, Chen Hong
Peking University People's Hospital

Objectives: Recent studies demonstrated that endothelial-derived microRNAs (miRNAs) can be detected in clinical plasma/serum samples, and there are also evidences indicated that inflammation disease states (e.g., atherosclerosis, cancer, etc.) may affect the levels of circulating miRNAs, but so far there is no direct proof about whether inflammation could induce endothelial cells to release miRNAs into circulation.This study aimed to explore whether inflammation could induce endothelial cells to release miRNAs into circulation and to investigate whether these released miRNAs derived from endothelial cells were transported in microparticles.
Methods: Microparticles were isolated from human atherosclerotic plaques with an active inflammatory phenotype and normal vascular tissue. Endarteretomy specimens constituting the intima and inner media of carotid atherosclerotic regions were obtained from the patients underwent carotid endarteretomy (CEA) (n=9). Patients undergoing coronary artery bypass surgery (CABG) procedure (n=9) were included as controls and the whole thickness vascular rings of normal vascular tissue (LIMA) were obtained. Flow cytometry and real time PCR were used to detect the levels of microparticles and microRNAs. To investigate whether these upregulated ECs-enriched miRNAs levels in the MPs isolated from atherosclerotic plaques were caused by inflammatory stimuli, human umbilical vein endothelial cells (HUVEC) were treated with TNF-α (TNF-α group, n=3) or DMEM (control group, n=3) for 24 hours. and then HUVEC and the culture medium were respectively collected.
Results: By comparing microparticles isolated from human atherosclerotic plaques with an active inflammatory phenotype (n=9) and those from normal vascular tissues (n=9), we found levels of annexin V+ microparticles and annexin V+ CD144+ microparticles were significantly increased in plaques (P <0.001) and angiogenesis-associated miRNAs (106b, 25, 92a and 21) were also significantly increased in microparticles from plaques (P <0.05). After exposure to TNF-α at a concentration of 10 ng/ml (TNF-α group, n=3) or DMEM (control group, n=3) for 24 hours, counts of microparticles and expressions of miRNAs-106b, 25, 92a and 21 in microparticles